



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/677,865	10/03/2003	Guy Bruno Rene Serre	016800-336	9835

21839 7590 04/11/2006

BUCHANAN INGERSOLL PC
(INCLUDING BURNS, DOANE, SWECKER & MATHIS)
POST OFFICE BOX 1404
ALEXANDRIA, VA 22313-1404

EXAMINER

ROBINSON, HOPE A

ART UNIT	PAPER NUMBER
----------	--------------

1656

DATE MAILED: 04/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/677,865

Applicant(s)

SERRE ET AL

Examiner

Hope A. Robinson

Art Unit

1656

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 January 2006.
- 2a) This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 18-25 and 28-33 is/are pending in the application.
- 4a) Of the above claim(s) 20-23 and 28-31 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 18, 19, 24, 25, 32 and 33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) ☒ Notice of References Cited (PTO-892) | 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) ☐ Notice of Informal Patent Application (PTO-152) |
| 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>7/15/05; 10/03/03</u> . | 6) ☐ Other: _____ |

DETAILED ACTION

Application Status

1. Applicant's response to the Office Action mailed October 6, 2005 on January 9, 2006, 2005, is acknowledged. The Terminal Disclaimer filed on January 9, 2006 has been received and entered.

Claim Disposition

2. Claims 32-33 have been added. Claims 18-25 and 28-33 are pending. Claims 18-19, 24-25 and 32-33 are under examination.

Sequence Compliance

3. The sequence amendment filed on January 9, 2006 has been received and entered. The application is now in compliance with the sequence rules.

Priority

4. As previously stated, applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119 (a-d) as follows: while applicant has claimed priority to France 97/03899, filed March 28, 1997 and France 97/11317, filed September 11, 1997, no certified copy is present in the application. The examiner cannot grant priority until said documents are received.

Art Unit: 1656

The response filed on January 9, 2006 stat that the Examiner acknowledged a copy of the priority document on June 3, 2003, in Paper No. 34 (see page 9 of the response). It is assumed that applicant is referring to the parent file, however, each application filed has to have a certified copy of the priority document and none was found in the instant application.

Withdrawn-Specification Objections

5. Previous objection to the specification are withdrawn by virtue of submission of an amendment.

Information Disclosure Statement

6. The information disclosure statements filed on October 3, 2003 and July 15, 2005 have been received and entered. The references cited on the PTO-1449 Form have been considered by the examiner and a copy is attached to the instant Office action.

New-Claim Objection

7. Claims 18 and 24 are objected to because of the following informalities:

Claim 18 is objected to for the recitation of "at least one protease active" instead of "at least one proteases".

For clarity and precision of claim language it is suggested that claim 24 is amended to recite "A cosmetic or pharmaceutical composition".

Correction of is required.

New-Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 18-19, 24-25 and 32-33 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Note that the claimed composition claims have been amended to recite "peptides" and "polypeptides", however, there is no clear indication that these are not products of nature. It is suggested that the claims are amended to recite "purified", "isolated" or "synthetic" in association with the claimed products and to demonstrate the hand of man.

New-Claim Rejections - 35 USC 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Art Unit: 1656

9. Claims 18-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed invention is directed to a composition comprising peptides obtained by the protease digestion of a polypeptide of SEQ ID NO:1, using an effective quantity sufficient to increase desquamation of at least one protease active on the polypeptide, said protease comprising Endoproteinase LysC, Endoproteinase GluC, Thrombin, pepsin, Myxobacter AL117 or Elactase (see for example claim 18). The claimed composition comprise a genus of peptides resulting from said digestion for which no structure is provided and for which the specification has not described possessing the asserted function. The skilled artisan cannot envision the detailed chemical structure of all the peptides encompassed in the claims, thus the claimed invention lacks adequate written description. Claim 18 and the instant specification provides a laundry list of protease for digestion to obtain the unspecified amounts of peptides. The specification does not provide information as to the potential cleavage sites of the enzymes or indicate what enzyme or mixtures of enzymes are used. The art recognizes that a potential cleavage site does not necessarily result in an actual cleavage site, as cleavage sites can be inaccessible. Klaus et al. describe cleavage sites that are not readily accessible to the mitochondrial processing peptidase that become cryptic and uncleaved protein accumulates *in vivo* in the mitochondrial matrix (page 859, right column). It is also stated that "...presequence, a cleavage site motif may be presented

Art Unit: 1656

in a conformation that allows processing by the mitochondrial processing peptidase while the same sequence inside of a protein could become part of a folded domain where it would no longer be accessible for the mitochondrial processing peptidase (page 860, left column). According to Klaus et al. cryptic cleavage sites are not uncommon. For example, Factor Xa of the blood clotting system efficiently cleaves prothrombin after the sequence motif IEGR ... In chimaeric fusion proteins, the same motif is cleaved with largely different efficiencies and in many cases, the site is not recognized..." (see Eur. J. Biochem. vol. 236, pages 856-861, 1996). In addition, the optimum condition of the enzyme is important, what order the enzymes are added to the digest and the activity of the enzymes (which enzyme is more active). Furthermore, substrate specificity plays a critical role. The instant specification provides three peptides, which is not representative of the peptides encompassed in the claims. The specification fails to provide any additional representative species of the claimed genus to show that applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, disclosure of drawings, or by disclosure of relevant identifying characteristics, for example, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

Art Unit: 1656

Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. In addition, there is not indication of what effective quantity is sufficient to increase desquamation in the instant specification. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir.1991), states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116). The skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993).

Therefore, for all these reasons the specification lacks adequate written description, and one of skill in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

10. Claims 18-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the protein set forth in SEQ ID NO: 1, does not

Art Unit: 1656

reasonably provide enablement for genus of peptides encompassed in the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The enablement requirement refers to the requirement that the specification describe how to make and how to use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: Quantity of Experimentation Necessary; Amount of direction or guidance presented; Presence or absence of working examples; Nature of the Invention; State of the prior art and Relative skill of those in the art; Predictability or unpredictability of the art and Breadth of the claims (see *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988)). The factors most relevant to the instant invention are discussed below.

The amount of experimentation required to practice the claimed invention is undue as the claims encompass an unspecified amount of peptides of SEQ ID NO: 1 following digestion with at least one protease listed in claim 18. The instant specification does not demonstrate or provide guidance as to what structure the peptides will have, thus the recitation of SEQ ID NO:1 does not rectify this deficiency in view of the laundry list of protease to be employed in a digest. The claims encompass digestion with a mixture of protease and it is unpredictable as to what fragments will result absent guidance as to the order of the protease added to the digest and the specificity of the substrate. For example, Proline-endopeptidase preferentially cleaves at

Art Unit: 1656

a proline in position P1, however, the P1 activity is blocked when another Pro is at position P1' (amino acid residues undergoing cleavage are designated P1, P2, P3, P4 etc. in the N-terminal direction from the bond cleaved and the bonds in the C-terminal direction are considered to be P1'), see for example residues P425 and P426 of SEQ ID NO:1. Looking at SEQ ID NO:1, Proline-endopeptidase could cleave the proline at position 458 or 485, however, another enzyme would need to be added to get a specific peptide fragment. A first and obvious approach to obtaining information concerning the cleavage specificity of a protease is the characterization of the respective natural substrate. Elastase and Myxobacter AL117 is not well characterized and were not found in the enzyme nomenclature. The art recognizes Elastase. Thus, significant further experimentation is required to determine the specificity of elastase and Myxobacter AL117 as the instant specification lacks guidance/direction. The derivation of the peptides encompassed in claim 18 depends on where a protein is cleaved by the protease and the susceptibility of the cleavage sites. According to Klaus et al. cryptic cleavage sites are not uncommon. For example, Factor Xa of the blood clotting system efficiently cleaves prothrombin after the sequence motif IEGR ... In chimaeric fusion proteins, the same motif is cleaved with largely different efficiencies and in many cases, the site is not recognized...". In addition, Klaus et al. describe cleavage sites that are not readily accessible to the mitochondrial processing peptidase that become cryptic and uncleaved protein accumulates *in vivo* in the mitochondrial matrix (page 859, right column), see Eur. J. Biochem. vol. 236, pages 856-861, 1996. A skilled artisan is essentially looking for a needle in a haystack absent guidance/direction as to the

Art Unit: 1656

protease cleavage sites and proteases added to the digest. Furthermore, as evidenced by the art potentially cleavage site does not equate to actual cleavage as cryptic cleavage sites are not uncommon. Due to the large quantity of experimentation necessary to generate the infinite number of peptides recited in the claims and possibly screen same for the specific activity (increase desquamation) and the lack of guidance/direction provided in the instant specification, this is merely an invitation to the skilled artisan to use the current invention as a starting point for further experimentation. Thus, undue experimentation would be required for a skilled artisan to make and/or use the claimed invention commensurate in scope with the claims. Moreover, the instant specification does not exemplify the peptides encompassed in the claims in a composition having the desired effect of "increase desquamation". Thus, the claimed invention is not commensurate in scope with the claims.

It is unpredictable to determine which peptides will result from a digest involving at least one protease recited in claim 18. The recitation of at least one does not put an upper limit on the number of mixtures that occur. The peptides resulting from the digest depends on the order that the enzyme is added in, which enzyme is more active, substrate specificity, and optimum condition for the enzymes. For example, thrombin would require different conditions than pepsin, which requires acidic conditions. The specification lacks guidance/direction as to the potential cleavage sites of the enzymes recited in the claims and a potential cleavage site does not equate to actual cleavage, as the site could be blocked or inaccessible. In addition, the peptide obtained may not be active or properly fold. Wells discloses that there are various sites or regions directly

Art Unit: 1656

involved in binding activity and in providing the correct three-dimensional spatial orientation of binding and active sites can be affected by altering the structure of proteins (Biochemistry, vol. 29, pages 8509-8517, 1990). No correlation is made between structure and function for the peptides encompassed in the claims.

The state of the prior art provides evidence for the high degree of unpredictability as stated above. The specification lacks adequate guidance/direction to enable a skilled artisan to practice the claimed invention commensurate in scope with the claims. The working examples provided do not rectify the missing information in the instant specification pertaining to the claimed variant. The nature and properties of this claim is difficult to ascertain from the examples provided as one of skill in the art would have to engage in undue experimentation to construct the variants of the claimed invention and examine the same for function.

The specification does not provide support for the broad scope of the claims, which encompass an unspecified amount of peptides resulting from digests using a laundry list of protease wherein the intended use of the composition is for a cosmetic or pharmaceutical. Critical to this process are actual cleavage sites and cleavage rates. The issue in this case is the breath of the claims in light of the predictability of the art as determined by the number of working examples, the skill level artisan and the guidance presented in the instant specification and the prior art of record. This make and test position is inconsistent with the decisions of *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) where it is stated that "...scope of claims must bear a reasonable correlation to scope of enablement provided by the specification to persons of ordinary

Art Unit: 1656

skill in the art...". Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988). Thus, for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention as the amount of experimentation required is undue, due to the broad scope of the claims, the lack of guidance and working examples provided in the specification and the high degree of unpredictability as evidenced by the state of the prior art, attempting to construct and test all peptides obtained in the claimed invention would constitute undue experimentation. Making and testing the infinite number of possible peptides to find one that functions as described is undue experimentation. Therefore, applicants have not provided sufficient guidance to enable one of skill in the art to make and use the claimed invention in a manner that reasonably correlates with the scope of the claims, to be considered enabling.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 18-19 and 32-33 are rejected under 112, second paragraph as failing to distinctly point out the subject matter applicant regards as his invention.

Art Unit: 1656

Claim 18 and the dependent claim hereto are indefinite for the recitation of "peptides obtained by the protease digestion of a polypeptide of SEQ ID NO:1, using an effective quantity, sufficient to increase desquamation, of at least one protease", because it is unclear what amount is considered to be sufficient and whether all possible peptides obtained will produce increase desquamation. In addition, the claim is indefinite as to Myxobacter AL117 and Elactase as the enzymes were not found in the enzyme nomenclature and are not well characterized in the art with respect to their potential cleavage sites.

Claims 32-33 lack clear antecedent basis for "the composition" as independent claim 24 recites "Cosmetic or pharmaceutical composition".

Maintained and Amended-Claim Rejections - 35 USC 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 24-25 and 32-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising the protein set forth in SEQ ID NO: 1 and the encoding DNA in SEQ ID NO:2, does not reasonably provide enablement for fragments thereof (see for example claims 24 and 33) or "all or a part thereof" (see for example claims 25 and 32) or a cosmetic/pharmaceutical composition employing said fragments/variants. The specification does not enable any

Art Unit: 1656

person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The enablement requirement refers to the requirement that the specification describe how to make and how to use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: Quantity of Experimentation Necessary; Amount of direction or guidance presented; Presence or absence of working examples; Nature of the Invention; State of the prior art and Relative skill of those in the art; Predictability or unpredictability of the art and Breadth of the claims (see *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988)). The factors most relevant to the instant invention are discussed below.

What is enabled are protein with specific sequence (SEQ ID NO: 1) and claims directed to "compositions" of the protein sequences *per se* but not "cosmetics" or "pharmaceuticals" employing fragments thereof. The specification has no cosmetics/pharmaceuticals for use in treating any skin disorders in association with the claimed fragments. The specification demonstrates possession of the claimed polypeptide and the encoding DNA, however, does not demonstrate possession of fragments of the DNA and the by products utilized in the claimed cosmetic or pharmaceutical composition to prevent a specific disorders. Additionally, there is no indication of dosage or time period for the claimed pharmaceutical composition or cosmetics. The encoding nucleic acid encompasses fragments, which could result in a

Art Unit: 1656

different protein that may not have biological activity. There is no indication of where in the sequence modifications will be made or any correlation between the structure and function relationship of the claimed product. Of note also is the fact that the specification does not provide any specific indicia of the composition in association with the laundry list of proteases listed.

In view of the foregoing, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. Furthermore, since the specification is absent exemplification of the therapeutic or cosmetic properties of the claimed invention the specification does not provide sufficient guidance to practice the claimed invention without undue experimentation. See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) a court decision that lists the factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue for further details. Furthermore, it is well known in the prior art that changes in a nucleotide sequence can have a dramatic affect on the protein product encoded by the sequence. While the degeneracy of the genetic code accommodates some variation in the nucleotide sequence, the extent of variation evident in applicant's claims go far beyond alternate codons for the same amino acid. For example, Tuddenham et al. (Nucleic Acids Research; vol. 22, no. 17, pages 3511-3533, 1994) discloses an established database of nucleotide substitutions, deletions, insertions and rearrangements. The database demonstrates

Art Unit: 1656

the deleterious impact that various point mutations, deletions and insertions have on the function of a Factor VIII protein. Furthermore, the reference demonstrates that a change of only a single nucleotide may result in loss of function in the protein product (see page 3512 of the reference). Additionally, Tuddenham et al. teach that substitution of an amino acid such as alanine, as a result of the changes to the nucleotide sequence, have a significant functional impact on the polypeptide. The changes to the nucleotide sequence described by Tuddenham et al. are limited in comparison to the wide degree of variability encompassed in the instant application. A skilled artisan would be led to expect that the variation in the polynucleotide sequence would at best code for a polypeptide that has impaired function and at worst be either nonfunctional or an entirely different product from that of the claimed invention. Therefore, the amount of experimentation necessary to determine which protein variants that have substantial homology with the native protein would have the same characteristics as the protein itself and if the protein subjected to the proposed variations would be functional or even the same product is beyond the scope of one with ordinary skill in the art. The instant application contains no guidance in performing these experiments, which adds to the difficulty in practicing the invention.

The specification does not provide support for the broad scope of the claims, which encompass an unspecified amount of variants/fragments of the encoding DNA. The claims broadly read on any fragment thereof/part thereof for the given sequence (SEQ ID NO: 2). The issue in this case is the breath of the claims in light of the predictability of the art as determined by the number of working examples, the skill level

Art Unit: 1656

artisan and the guidance presented in the instant specification and the prior art of record. This make and test position is inconsistent with the decisions of *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) where it is stated that "...scope of claims must bear a reasonable correlation to scope of enablement provided by the specification to persons of ordinary skill in the art...". Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

Thus, for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention as the amount of experimentation required is undue, due to the broad scope of the claims, the lack of guidance and working examples provided in the specification and the high degree of unpredictability as evidenced by the state of the prior art, attempting to construct and test fragments/variants of the claimed invention would constitute undue experimentation. Making and testing the infinite number of possible fragments/variants to find one that functions as described is undue experimentation. Therefore, applicants have not provided sufficient guidance to enable one of skill in the art to make and use the claimed invention in a manner that reasonably correlates with the scope of the claims, to be considered enabling.

13. Claims 24-25 and 32-33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as

Art Unit: 1656

to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed invention is directed to a cosmetic or pharmaceutical composition wherein the nucleotide sequence comprises "an active fragment thereof" or "all or part of" the nucleotide sequence in SEQ ID NO:2. The claims lack adequate written description with regard to the structure herein as there is no indicia as to what part of SEQ ID NO:2 is intended. In addition, the claims use the open language "comprising" which means more nucleotides can be added to the sequence. Thus, the claimed invention consist of a genus of fragments to the specified sequence. A skilled artisan cannot envision the detailed chemical structure of the nucleic acid. The specification fails to provide any additional representative species of the claimed genus to show that applicant was in possession of the claimed genus.

A representative number of species means that the species, which are adequately described are representative of the entire genus. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, disclosure of drawings, or by disclosure of relevant identifying characteristics, for example, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. Additionally, the instant specification lacks adequate written description with regard to the claimed cosmetic/pharmaceutical composition. The specification does

Art Unit: 1656

not adequately describe the claimed cosmetic or pharmaceutical composition with regard to dosage, treatment regimen, timing of treatment nor provide any data on humans or veterinary subjects for whom the pharmaceutical composition is directed. Absent adequate description, it is unclear how one skilled in the art would be able to practice the invention as claimed since the specification provides no data via examples or figures of an animal model to demonstrate the claimed cosmetic or pharmaceutical composition.

Further, *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir.1991), states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116). The skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993). Therefore, the claimed invention lacks adequate written description.

Withdrawn-Claim Rejections - 35 USC 112

14. Previous rejections to claims under 35 U.S.C. 112, second paragraph are withdrawn by virtue of submission of an amendment.

Withdrawn-Claim Rejections - 35 USC 112

15. Previous rejection to claims under 35 U.S.C. 103, Obvious-type Double Patenting is withdrawn by virtue of submission of a Terminal Disclaimer.

New-Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claim 18 is rejected under 35 U.S.C. 102(b) as being anticipated by SIGMA Chemical Company (SIGMA Catalog: Biochemicals Organic Compounds for Research and Diagnostic Reagents, 1994), based on the broad recitation of active "peptides obtained by the protease digestion of a polypeptide of SEQ ID NO:1".

The SIGMA catalog (on page 132, left column, compound A6911) discloses Arg-Ala (Acetate salt) used for research purposes or as a diagnostic reagent, which would inherently require mixture with water (composition). The Arg-Ala dipeptide can be obtained from SEQ ID NO:1 of the instant invention following protease digestion with

Art Unit: 1656

Thrombin (potential cleavage site is Arg) and Proline-Endopeptidase (potential cleavage site is Pro); see residues 5-7 of SEQ ID NO:1. As the claim reads on any polypeptide of SEQ ID NO:1 subjected to digest with at least one protease and asserts an activity for all the peptides encompassed, the limitations of the claims are met by this reference, said function would be an inherent property.

17. Claims 24-25 and 32-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhou et al. (PNAS, vol. 90, pages 9470-9474, 1993), based on the broad recitation of active fragment thereof.

Zhou et al. teach a gene and the encoding protein that is structurally similar to the protein the encoding DNA set forth in SEQ ID NO:1 and 2, respectively (see the attached alignment and pages 9470 and 9472 of the reference). The sequence set forth in the reference would be construed as an active fragment thereof, note that the instant specification does not provide a definition for the phrase. In addition, Zhou et al. disclose that protein is derived from the granular-cell layer of the epidermis and the role of the protein an association with psoriasis vulgaris (a disorder of keratinocyte proliferation). Based on the similarity in the structures of the products disclosed in the Zhou et al. reference with the instant sequences, claims 25, 32 and 33 are anticipated as the claim does not set forth what part of the structure is needed. Therefore, the limitations of the claims are met by the reference.

Response to Arguments

Art Unit: 1656

18. The response filed on January 9, 2006 has been considered, however, is not fully persuasive. Note that new grounds of rejections have been instituted under 35 U.S.C. 112, first and second paragraphs, and 102(b) for the reasons stated above because of amendments made to the claims. In addition, the rejections under 35 U.S.C. 112, first paragraph remains, however, has been amended to reflect amendments made to the claims. Note also that a new ground of rejection has been instituted under 35 U.S.C. 101, because the claims as amended do not clearly demonstrate the hand of man (and inserting "purified or synthetic" in association with the peptide/polypeptide would be consistent with the parent file (U.S. Patent No. 6,645,509).

On page 10 of the response applicant state that the rejection under 35 U.S.C. 112, first paragraph enablement is traversed because the examiner admits that the specification is enabled for SEQ ID NO:1. This argument is not persuasive as credit is given to the full-length sequence, however, the office action is stating that applicant is not enabled for fragments of the sequences in association with a cosmetic/pharmaceutical. In other words the product of SEQ ID NO:1 and 2 are enabled and a composition comprising SEQ ID NO:1 is enabled, however, a composition with the intended use of a cosmetic or pharmaceutical with a partial structure is not enabled by the instant disclosure. Applicant states that claims 18 and 19 have been amended to advance prosecution. Note that claims 24-25 and newly submitted claims 32-33 have the issues raised thus the enablement rejection of record stands, however, has been amended to reflect changes made to the claims. Applicants point to pages 11-15 of the specification which reports that the composition is intended for treating the thinning of

Art Unit: 1656

the epidermis, in particular the horny layer and treating excessive fragility of the skin. In addition, pages 12+ provide additional postulates of intended use and a laundry list of proteases. Applicant's comments regarding dosing has been considered but is not persuasive. The issue at hand is what is stated, what is demonstrated and what the breath of the claims encompass. There is no demonstration of said cosmetic or pharmaceutical composition having the purported uses/effects employing the fragments. Therefore, the rejection remains.

With regard to the rejection under 35 U.S.C. 112, first paragraph, written description, applicant state that claim 25 has been amended and new claims 32 and 33 have been added to obviate this ground of rejection. Note that the rejection remains, however, has been amended to reflect changes made to the claims. Claim 24 has been added to the rejection as the claim as amended recites "an active fragment thereof". Contrary to applicant's statements claim 25 was not amended to remove the language rejected. Claim 25 and newly submitted claims 32-33 recites "all or part of the nucleotide sequence of SEQ ID NO:2" and "fragment of SEQ ID NO:2". This language does not obviate the grounds of rejection made but instead is precisely the reasoning for the rejection of record, therefore, rejection remains for the reasons stated above.

Conclusion

19. No claims are presently allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr, can be reached at (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hope Robinson, MS *HR*
Patent Examiner *3/31/06*

**HOPE ROBINSON
PATENT EXAMINER**

* DO NOT REMOVE - PART OF OFFICE ACTION *

GenCore version 5.1.6
Copyright (c) 1993 - 2005 CompuGen Ltd.

OM protein - protein search, using om model

Run on: August 2, 2005, 08:59:02, Search time 42 Seconds

(without alignment)

Title: US-10-677-865-1

Perfect score: 2752

Sequence: 1 MGSRAPMWGRVGRGHWL.....GQLADPBYVLPQGLDLPF 529

Scoring table: BLOSUM62

Gapop 10.0, Gapext 0.5

Searched: 283416 seqs, 96216763 residues

Total number of hits satisfying chosen parameters: 283416

Minimum DB seq length: 0

Maximum DB seq length: 200000000

Post-processing: Minimum Match 0%

Maximum Match 100%

Listing first 45 summaries

Database:

1: p1r1.*

2: p1r2.*

3: p1r3.*

4: p1r4.*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	DB ID	Description
1	2583	93.9	502	2	A48679
2	335	12.2	13288	2	T03099
3	330.5	12.0	1032	2	T34433
4	330.5	12.0	2232	2	T34433
5	328.5	11.9	1428	2	T08852
6	306.5	11.1	967	2	S66852
7	299.5	10.9	1585	2	T31611
8	292.5	10.6	528	2	I47141
9	289.5	10.5	1063	2	A86731
10	274.5	10.0	481	2	A35628
11	272	9.9	1275	2	T33359
12	263	9.6	286	2	C61635
13	260	9.4	534	2	T39003
14	257	9.3	1459	2	T02271
15	254	9.2	1560	2	T02885
16	253.5	9.2	1217	2	S52744
17	250.5	9.1	536	2	T37544
18	248.5	9.0	383	2	T46707
19	248.5	9.0	3507	2	T44513
20	248	9.0	1367	2	A48478
21	244	8.9	627	2	A44112
22	241.5	8.8	316	1	A38743
23	241.5	8.8	786	2	T16509
24	240.5	8.7	805	2	T35795
25	238.5	8.7	406	2	G38170
26	238	8.6	683	2	A62704
27	236.5	8.6	1464	2	S59856
28	235.5	8.6	995	2	S50358
29	233	8.5	1896	1	RMPFZL

30	231.5	8.4	1932	1	A28490	DNA-directed RNA p
31	230	8.4	1414	1	S23809	collagen alpha 2(I)
32	230	8.4	1589	2	T42233	submaxillary mucin
33	229.5	8.3	539	2	T28770	hypothetical prote
34	229	8.3	725	2	A41258	a-aggutinin core
35	226.5	8.2	2468	2	A03412	hypothetical prote
36	224	8.1	1777	2	T34369	hypothetical prote
37	223.5	8.1	1306	2	S25370	MSB2 protein - yea
38	223	8.1	467	2	A47677	DNA-directed RNA p
39	223	8.1	4776	2	B59206	cell wall surface
40	221.5	8.0	888	2	T46726	secreted acid phos
41	221	8.0	1970	1	S21054	DNA-directed RNA p
42	221	8.0	1970	2	T38186	RNA polymerase II
43	219.5	8.0	1475	2	G42718	nuclear pore compl
44	219	8.0	937	2	S58135	hypally regulated
45	218	7.9	1162	2	U05557	exo-alpha-glucosidase

ALIGNMENTS

RESULT 1

A48679 differentiated keratinocyte 5 protein precursor - human

C:Species: Homo sapiens (man)

C>Date: 03-May-1994 #sequence_revision 03-May-1994 #text_change 09-Jul-2004

C/Accession: A48679

R/Zhou, Y.; Chaplin, D.D.

Proc. Natl. Acad. Sci. U.S.A. 90, 9470-9474, 1993

A/Title: Identification in the HLA class I region of a gene expressed late in keratino

A/Reference number: A48679; MUID:94022396; PMID:8415725

A/Accession: A48679

A/Status: preliminary

A/Molecule type: mRNA

A/Releaser: 1-502 <CHO>

A/Cross-reference: UNIPROT:043509; GB:120815

A/Note: sequence shown follows the authors' translation at positions 47 and 410

C/Genetic:

A/Map position: 6p21.3

A/Superfamily: Iorlorin

Query Match	Score	Length	DB 2	Matches	Conservative	Mismatches	Indel	Gap	0
Qy	1	502	2	1	1	0	0	0	0
Db	1	502	2	1	1	0	0	0	0
Qy	61	502	2	61	61	0	0	0	0
Db	61	502	2	61	61	0	0	0	0
Qy	121	502	2	121	121	0	0	0	0
Db	121	502	2	121	121	0	0	0	0
Qy	181	502	2	181	181	0	0	0	0
Db	181	502	2	181	181	0	0	0	0
Qy	241	502	2	241	241	0	0	0	0
Db	241	502	2	241	241	0	0	0	0
Qy	301	502	2	301	301	0	0	0	0
Db	301	502	2	301	301	0	0	0	0
Qy	361	502	2	361	361	0	0	0	0
Db	361	502	2	361	361	0	0	0	0

GenCore version 5.1.7
Copyright (c) 1993 - 2006 Bioacceleration Ltd.

OM nucleic - protein search, using frame_plus_n2p model

Run on: March 21, 2006, 22:20:04 ; Search time 6.8 Seconds

(without alignments)
4499.549 Million cell updates/sec

Title: US-10-677-865A-2

Perfect score: 528

Sequence: 1 atggggccgcgtcgcggcacc.....agttactcgcagatccataa 1590

Scoring table:
OLIGO
Xgapop 60.0 , Xgapext 60.0
Ygapop 60.0 , Ygapext 60.0
Fgapop 6.0 , Fgapext 7.0
Delop 6.0 , Delext 7.0

Searched: 283416 seqs, 96216763 residues

Word size: 1

Total number of hits satisfying chosen parameters: 565918

Minimum DB seq length: 0

Maximum DB seq length: 200000000

Post-processing: listing first 50 summaries

Command line parameters:

-MODEL=frame+ n2p.model -DEV=x1h
-Q=/abs/ASSWEB/spool/US10677865/runat.21032006.152106.26838/app.query.fasta_1
-DB=PIR -OPMT=fastan -SUFFIX=coligo.rpr -MINMATCH=0.1 -LOOPEL=0 -LOOPEXT=0
-UNITS=bits -STRAT=1 -END=1 -MATRIX=oligo -TRANS=human40.cdi -LIST=50
-DOCALLIGN=200 -THR SCORE=quality -THR MIN=1 -ALIGN=75 -MODE=LOCAL -OUTFMT=pro
-NOR=ext -HEAPSIZE=500 -MINLEN=0 -MAXLEN=200000000 -HOST=abs805h
-USER=US10677865 @CGN 1 1 25 @runat.21032006.152106.26838 -NCPU=6 -ICPU=3
-NO MMAP -NEG SCORES=0 -WAIT -DSPBLOCK=100 -LONGLOG -DEV TIMEOUT=120
-WARN TIMEOUT=30 -THREADS=1 -XGAPOP=60 -XGAPEXT=60 -FGAPOP=6 -FGAPEXT=7
-YGAPOP=60 -YGAPEXT=60 -DELOP=6 -DELEXT=7

Database: PIR_80.*

1: pir1.*
2: pir2.*
3: pir3.*
4: pir4.*

Prod. No. is the number of results predicted by chance to have a
score greater than or equal to the score of the result being printed,
and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	DB ID	Description
1	224	42.4	502	2 A48679	differentiated ker
2	12	2.3	733	2 S44876	ZC21.4 protein - C
3	11	2.1	698	2 A84547	hypothetical prote
4	10	1.9	206	2 T23852	hypothetical prote
5	10	1.9	344	2 T40167	hypothetical prote
6	10	1.9	365	2 A49235	outer membrane lip
7	10	1.9	375	2 D87427	conserved hypothet
8	10	1.9	710	2 S28014	outd protein - ER
9	9	1.7	167	2 T47385	hypothetical prote
10	9	1.7	277	2 D84596	hypothetical prote
11	9	1.7	299	2 T12483	hypothetical prote
12	9	1.7	345	2 B43731	achaeae-scute comp
13	9	1.7	356	2 JX0141	cytochrome-c oxida
14	9	1.7	357	2 P96708	hypothetical prote

15	9	1.7	367	2 I39649	lipoprotein - Acti
16	9	1.7	406	2 G96497	hypothetical prote
17	9	1.7	427	2 C88883	protein JG8.10 [m
18	9	1.7	427	2 A32372	female-specific do
19	9	1.7	441	2 G01758	transcription fact
20	9	1.7	450	2 C95348	HemM copriophyri
21	9	1.7	452	2 T40634	hypothetical prote
22	9	1.7	453	2 T48240	hypothetical prote
23	9	1.7	465	2 F75524	hypothetical prote
24	9	1.7	474	2 I38240	transcription fact
25	9	1.7	510	2 T37541	probable glycolip
26	9	1.7	549	2 B32372	male-specific doub
27	9	1.7	623	1 S3167	gene pointed prote
28	9	1.7	644	2 S39356	transcription fact
29	9	1.7	683	2 A82704	1,4-beta-cellobios
30	9	1.7	837	2 D84428	hypothetical prote
31	9	1.7	1065	2 T13230	dachshund isoform
32	9	1.7	1072	2 T13232	dachshund protein
33	9	1.7	1074	2 T13229	dachshund protein
34	9	1.7	1081	2 T13231	dachshund protein
35	9	1.7	1139	2 B54962	sterol regulatory
36	9	1.7	1337	2 T38949	hypothetical prote
37	9	1.7	1428	2 T08852	lutein A - Califo
38	9	1.7	1469	2 T09219	basal transcriptio
39	9	1.7	1785	2 A45546	major merizolite su
40	9	1.7	3972	2 S75251	hypothetical prote
41	8	1.5	89	2 T45015	hypothetical prote
42	8	1.5	97	1 ERBP12	gene 1C protein -
43	8	1.5	99	2 D86931	hypothetical prote
44	8	1.5	100	2 A72572	hypothetical prote
45	8	1.5	115	2 D61615	sericin MG-1 - gre
46	8	1.5	120	2 T45451	hypothetical prote
47	8	1.5	120	2 A45519	variant surface gl
48	8	1.5	125	2 S69871	hypothetical prote
49	8	1.5	129	2 T00282	hypothetical prote
50	8	1.5	141	2 A86417	probable auxin-ind

ALIGNMENTS

RESULT 1

A48679 differentiated keratinocyte S protein precursor - human

C:Species: Homo sapiens (man)
C:Date: 03-May-1994 #sequence_revision 03-May-1994 #text_change 09-Jul-2004

C:Accession: A48679
R:Zhou, Y.; Chaplin, D.D.

Proc. Natl. Acad. Sci. U.S.A. 90, 9470-9474, 1993
A:Title: Identification in the HLA class I region of a gene expressed late in keratin

A:Reference number: A48679; MUID:94022396; PMID:8415725
A:Accession: A48679

A:Status: preliminary
A:Molecule type: mRNA

A:Residues: 1-502 <ZHO>
A:Cross-references: UNIPROT:O43509; UNIPARC:UPI0000177376; GB:L20815

A:Note: Sequence shown follows the authors' translation at positions 47 and 410
C:Genetics:
C:Map position: 6p21.3

C:Superfamily: lorixin

Alignment Scores:

Prod. No.: 2.02e-205 Length: 502
Score: 224.00 Matches: 224
Percent Similarity: 100.0% Conservative: 0
Best Local Similarity: 100.0% Mismatches: 0
Query Match: 42.4% Indels: 0
DB: 2 Gaps: 0

US-10-677-865A-2 (1-1590) x A48679 (1-502)

QY 550 CGCGAATACCTAAACCTTCCACAGCTGAGCAAGACTTCTCTCCCAACCTGAG 609
DB 184 ArgGylleuamProserGlnProGlyInserSerSerSerGlnThrSerly 203

QY	610	GTATCCAGCAGTGGGCCAAAGGCTCAGCTCCAAACGAGGTCCTCGTATGTTGGACATCCCC	669
Db	204	ValSerSerSerSerGlyGlnSerValSerSerSerGlnArgProCysSerSerSerIlePro	223
QY	670	GACTCTCCCTGACAGTGAAGGAGCCCATGCTCTGCACTCTTGAGCCCTACATCCCAAGCTCC	729
Db	224	AspSerProCysSerSerGlyGlyProIleValSerHisSerGlyProTyrIleProSerSer	243
QY	730	CACCTCTGTGCAGGGGGGTCAAGGCTCTGTGTGTGTGTGGACCAAGCAGCGTTCTGGT	789
Db	244	HisSerValSerGlyGlyGlnArgProValValValValAlaAspGlnHisGlySerGly	263
QY	790	GCCCCCTGAGGAGGTTCAAAGGTCGCCCTGTAGCAATGTTGGCCTTCCAGGCAAGCCCTGT	849
Db	264	AlaProIleValValGlnGlnGlyProProCysSerSerHisGlyLeuProGlyLysProCys	283
QY	850	CCCCCAATCACTCTGTAGCAAAATCCTATGTTGGTCTACAGAGTGTGGTGGTCTCTCT	909
Db	284	ProIleIleHisSerValAlaPheLysSerTyrGlyGlyGlnValValGlyGlySerSer	303
QY	910	GACAGTATCTGCTGTTCAGAGCAATCACTACAGTAAAGGTAAATCTATCCTGTGGGCTAC	969
Db	304	AspSerTyrLeuValProGlyMetThrLysSerLysGlySerIleTyrProValGlyTyr	323
QY	970	TTCAACAAGAGAACCCTGTGAAGGCTCTCAAGGGGTCCCTTCTTTGACAGCTGGGACC	1029
Db	324	PheThrLysGlnLeuAsnProValLysGlySerProGlyValProSerPheHisAlaGlyPro	343
QY	1030	CCCATCTCTGAGGGCAAAATCTTCTCCAGCAACCCCATCATCCCAAGCAGCTGGCAACT	1089
Db	344	ProIleSerGlnGlyLysTyrPheSerSerSerAsnProIleIleProSerGlnSerAlaAla	363
QY	1090	TCCCTGGCCATGTGGGTTCCAGCCAGTGGGAGCATGTTGGGCTCCAGGCTGTGTGAGGCGGC	1149
Db	364	SerSerAlaIleAlaPheGlnProValGlyThrGlyValGlnMetCysGlyGlyGly	383
QY	1150	TCCACGGGCTCCAAAGGACCTGTCTCTCCCTCCAGTTCAGATCCCAAGCAAGTTTAC	1209
Db	384	SerThrGlySerLysGlyProCysSerProSerSerSerArgValProSerSerSerSer	403
QY	1210	ATTCCAGCAGC 1221	
Db	404	IleSerSerSer 407	

```

RESULT 2
S44876
ZC21.4 protein - Caenorhabditis elegans.
C/Species: Caenorhabditis elegans
C/Date: 14-Sep-1994 #sequence_revision 12-May-1995 #text_change 23-Mar-2001
C/Accession: S44876
R/Du, Z.; Watson, R.
submitted to the EMBL Data Library, May 1993
A/Description: Sequence of the C. elegans cosmid ZC21.
A/Reference number: S44649
A/Accession: S44876
A/Status: preliminary
A/Molecule type: DNA
A/Residues: 1-733 <DNUZ>
A/Cross-references: UNIPARC:UP1000017BD58; EMBL:L16685; NID:G289729; PID:G289735
C/Genetics:
A/Introns: 269/3; 551/3; 600/2; 670/3

Alignment Scores:
Pred. No.:          0.0129      Length:      733
Score:              12.00       Matches:     12
Percent Similarity: 100.0%     Conservative: 0
Best Local Similarity: 100.0%  Mismatches: 0
Query Match:        2.3%       Indels:     0
DB:                  2          Gaps:       0

US-10-677-865A-2 (1-1590) x S44876 (1-733)

```

```

OY      250 TCTGGTGTGGTCCAGAGTAGCTCCAGCGAATCC 285
          |||||
DB      50 SerGlyGlyGlySerSerGlySerSerGlySer 61

```

RESULT 3

Hypothetical protein AC2g17010 [imported] Arabidopsis thaliana
 C|Species: Arabidopsis thaliana (mouse-ear cress)
 C|Date: 02-Feb-2001 #sequence_revision 02-Feb-2001 #next_change 09-Jul-2004
 C|Accession: AB44547
 R|Lin, X.; Kall, S.; Rounsley, S.D.; Shea, T.P.; Benito, M.I.; Town, C.D.; Fujii, C.Y.
 M.; Koo, H.; Moffatt, K.S.; Cronin, L.A.; Shen, M.; Vanden, S.B.; Umayam, L.; Tallon,
 euss, D.; Nleman, W.C.; White, O.; Eisen, J.A.; Salzberg, S.L.; Frazer, C.M.; Venter
 Nature 402, 761-768, 1999
 A|Title: Sequence and analysis of chromosome 2 of the plant Arabidopsis thaliana.
 A|Reference number: AB44547; PMID:20083487; PMID:10617197
 A|Accession: AB4547
 A|Status: preliminary
 A|Molecule type: DNA
 A|Residues: 1-698 <STO>
 A|Cross-references: UNIPROT:Q7XJL9, UNIPARC:UPI000016233B, GB:AE002093, NID:96598358;
 C|Genetics:
 A|Gene: AC2g17010
 A|Map position: 2

Alignment Scores:	
Pred. No.:	639
Length:	0.118
Score:	11.00
Percent Similarity:	100.0%
Best Local Similarity:	100.0%
Query Match:	2.1%
DB:	2
Length:	639
Matches:	11
Conservative:	0
Mismatches:	0
Indels:	0
Gaps:	0

US-10-677-865A-2 (1-1590) X A84547 (1-698)

```

Oy      448 AGCAGCAGCTCTCATTGAGCAGCAGCAGCAGC 480
          |||||
Db      196 SerSerSerSerHisSerSerSerSerSer 206

```

RESULT 4

hypothetical protein R02D5.1 - *Caenorhabditis elegans*
 C/Species: *Caenorhabditis elegans*
 C/Date: 15-Oct-1999 #sequence_revision 15-Oct-1999 #next_change 05-Jul-2004
 C/Accession: T23852
 R/Mathews, L.
 submitted to the EMBL Data Library, August 1996
 A/Reference number: Z19808
 A/Accession: T23852
 A/Status: preliminary; translated from GB/EMBL/DBJ
 A/Molecule type: DNA
 A/Residues: 1-206 <NIL>
 A/Cross-references: UNIPROT:Q21636; UNIPARC:UP10000007FP99; EMBL:Z78015; PIDN:CAB01433
 A/Experimental source: clone R02D5
 C/Genetics:
 A/Gene: CBSP.R02D5.1
 A/Map position: 5
 A/Introns: 53/3

Alignment Scores:	
Pred. No.:	1.32
Score:	10.00
Percent Similarity:	100.0%
Best Local Similarity:	100.0%
Query Match:	1.9%
DB:	2
Length:	206
Matches:	10
Conservative:	0
Mismatches:	0
Indels:	0
Gaps:	0

US-10-677-865A-2 (1-1590) x T23852 (1-206)

```

Oy      451 AGCAGCTTCATTGCAGCAGCAGCAGC 480
      |||||
Db      84 SerSerSerHisSerSerSerSerSer 93

```